

**Figure 1B: siNA Hybridization Assay**

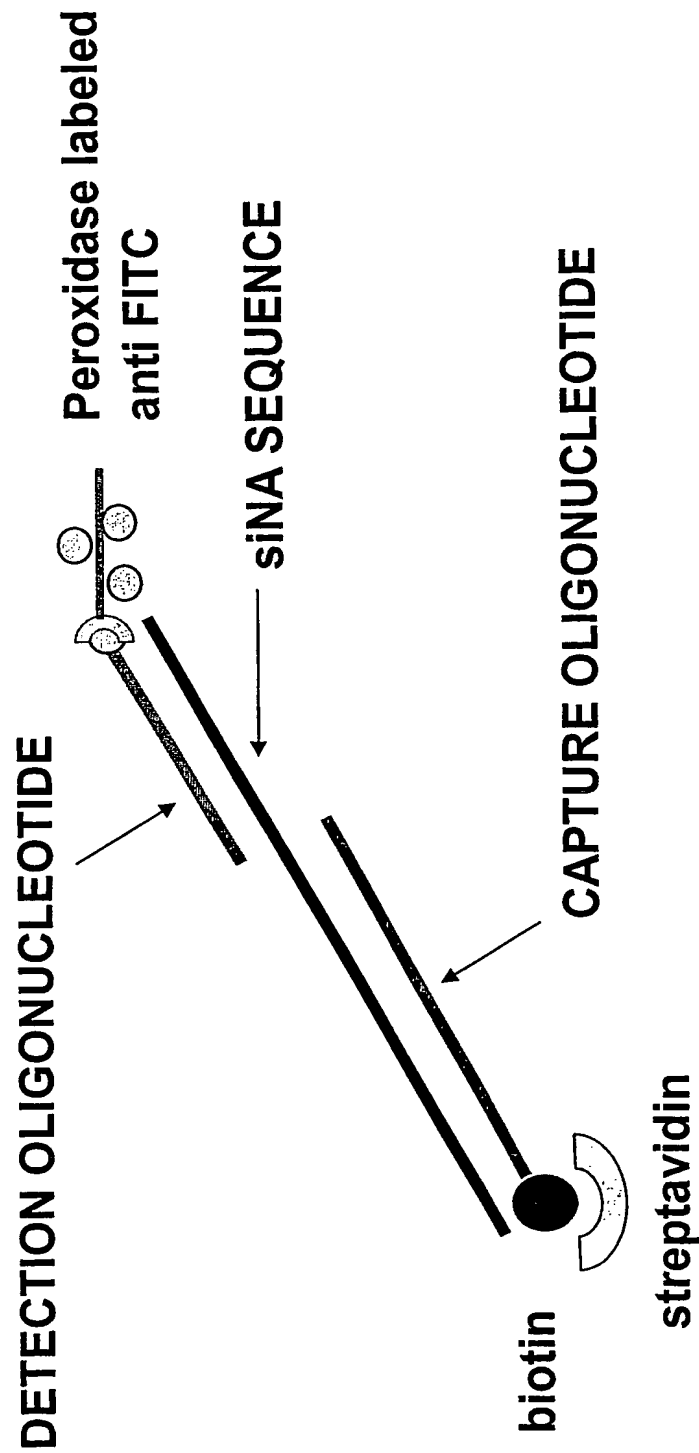
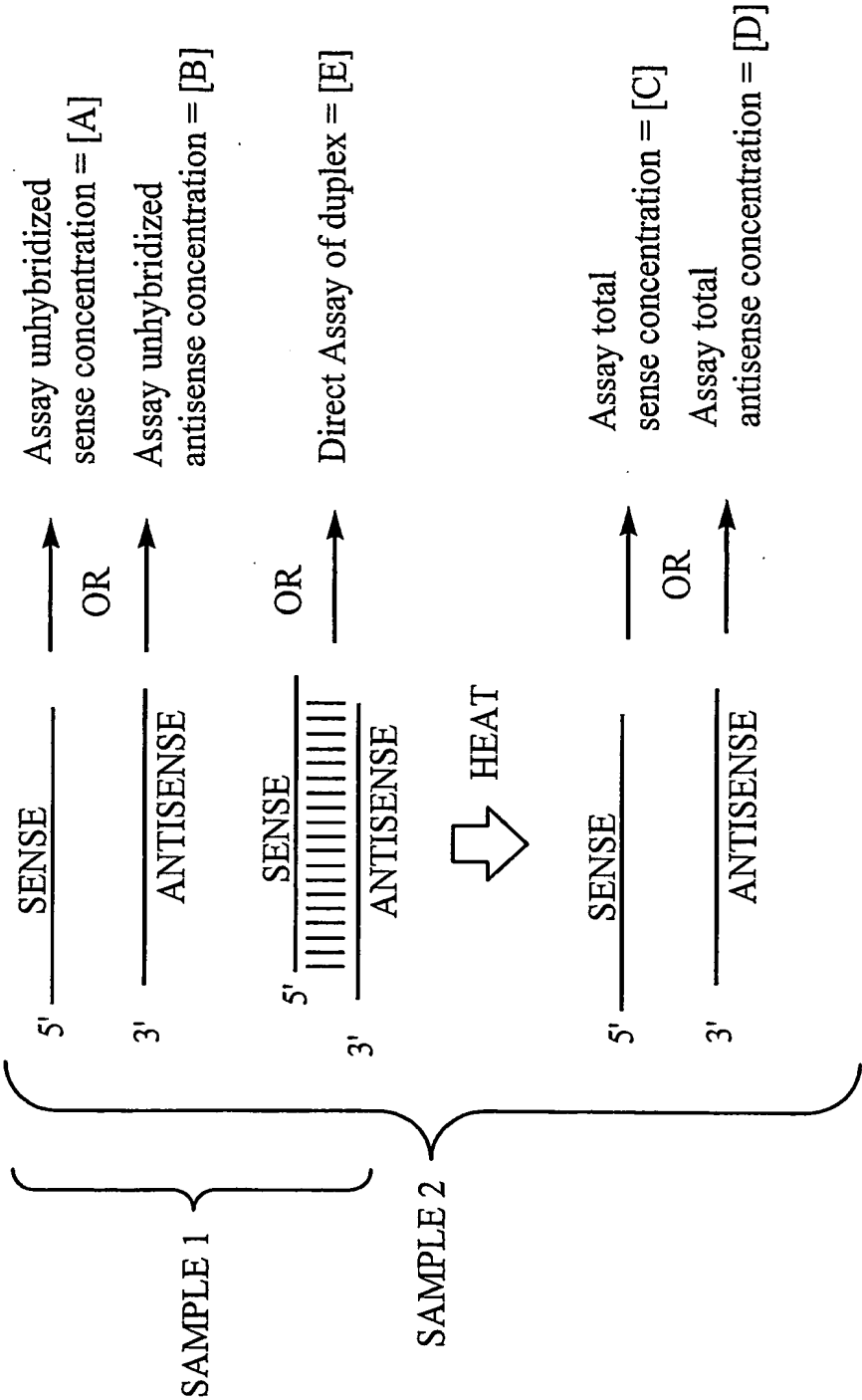
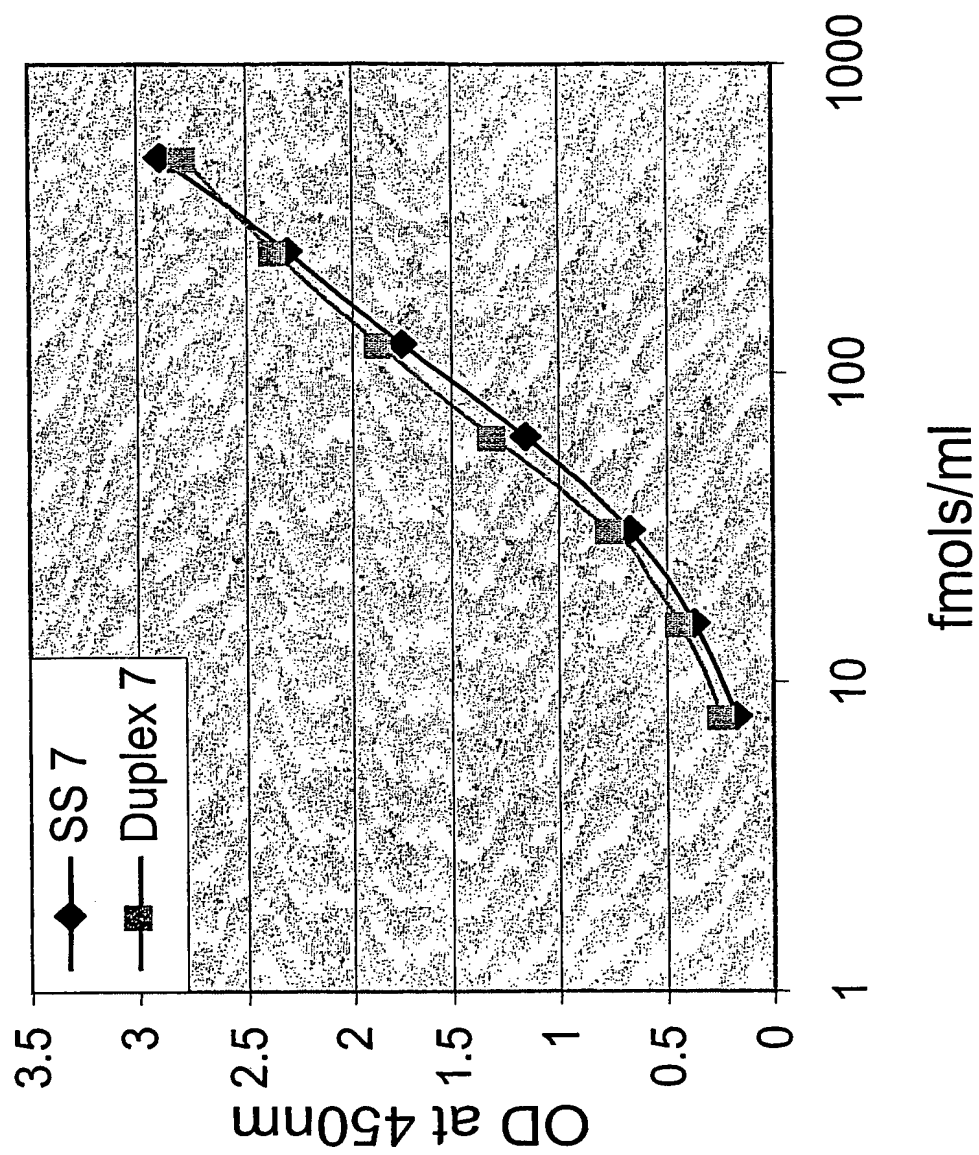


Figure 1C: Principle of siNA detection/quantitation Assays



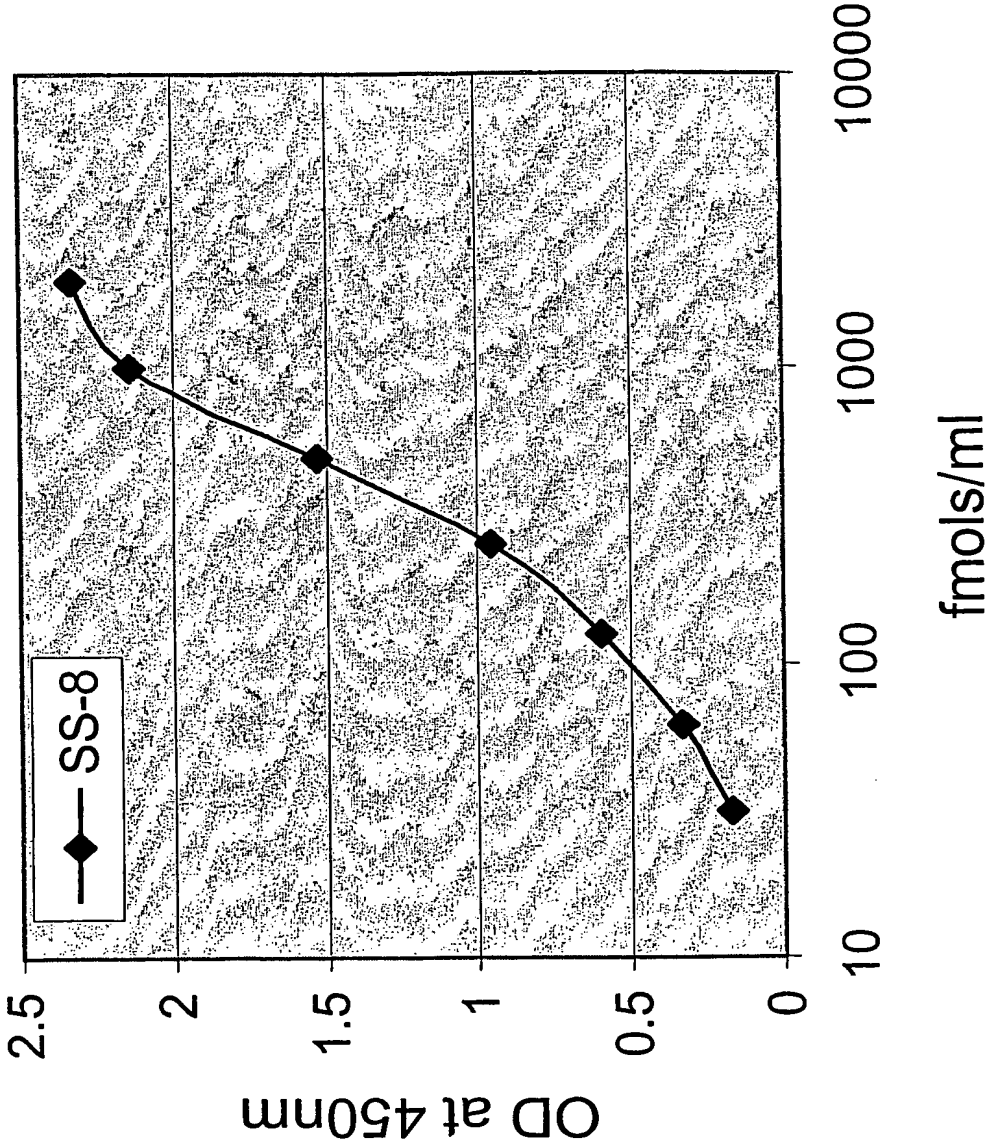
$[C] - [A] = [\text{Duplex}]$  based upon analysis of sense strand  
 $[D] - [B] = [\text{Duplex}]$  based upon analysis of antisense strand  
 $[E] = [\text{Duplex}]$  based upon direct analysis of duplex

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**Figure 2A: siNA Stab 7 Sense Strand Standard Curve**

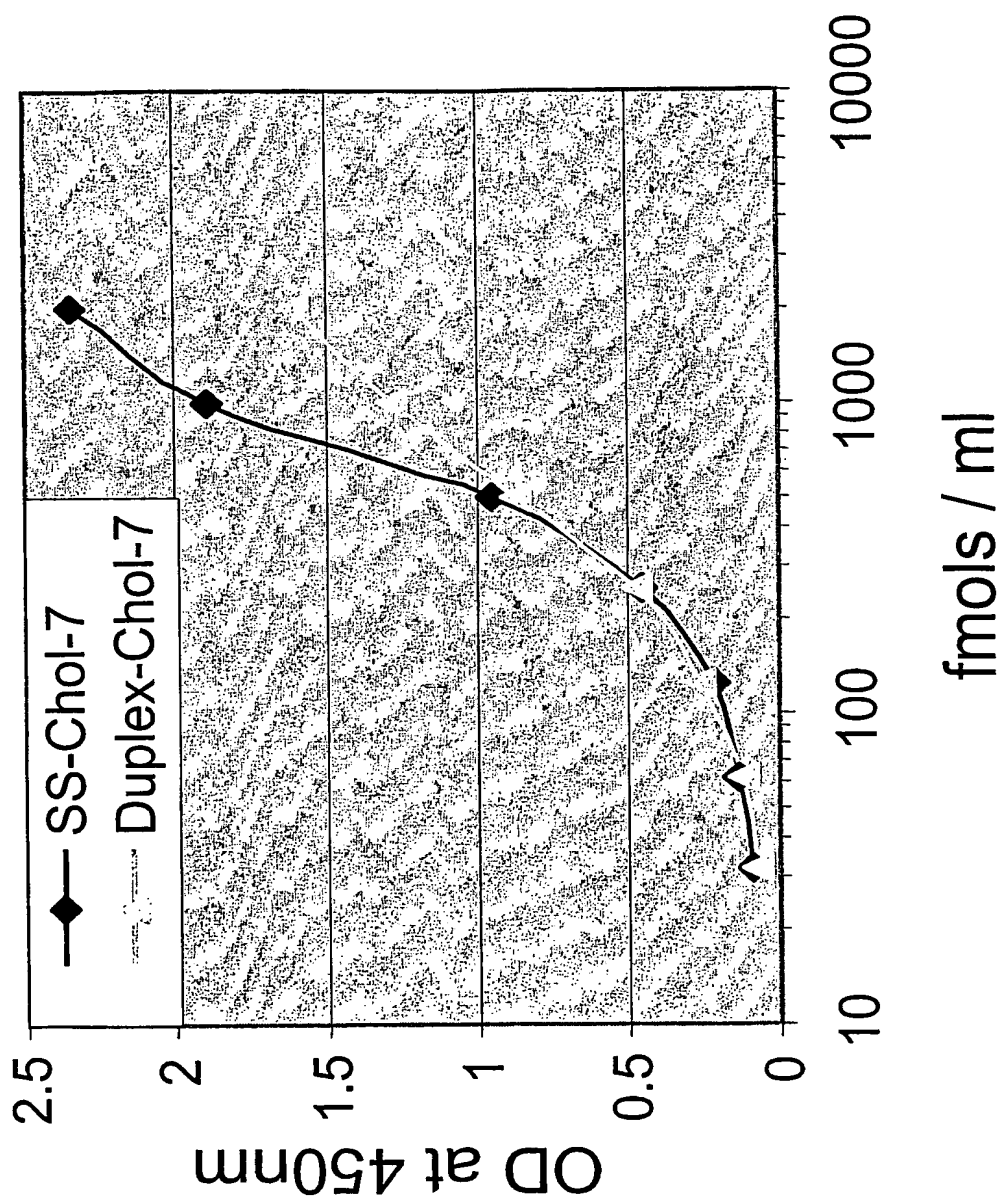
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Figure 2B: siNA Stab 8 Antisense Strand Standard Curve



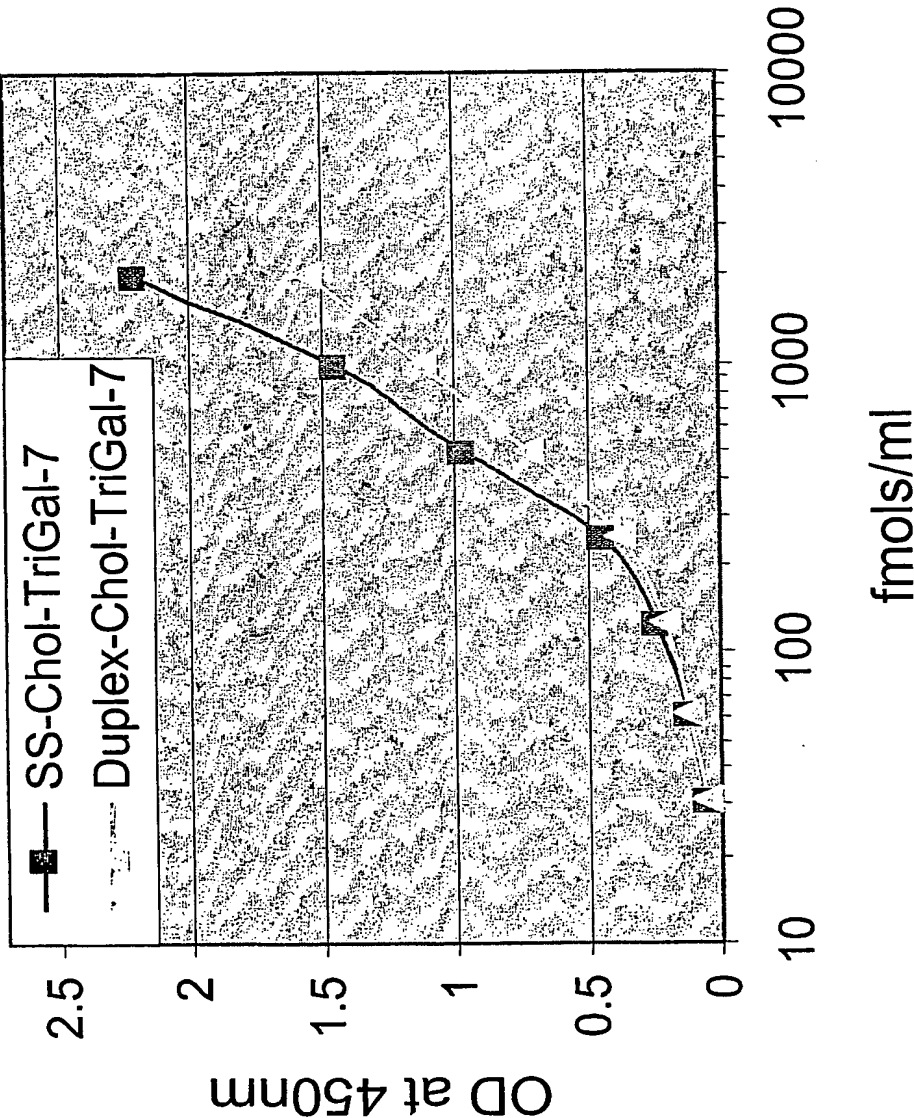
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**Figure 2C: siNA Stab 7 Cholesterol Conjugate  
Sense Strand Standard Curve**



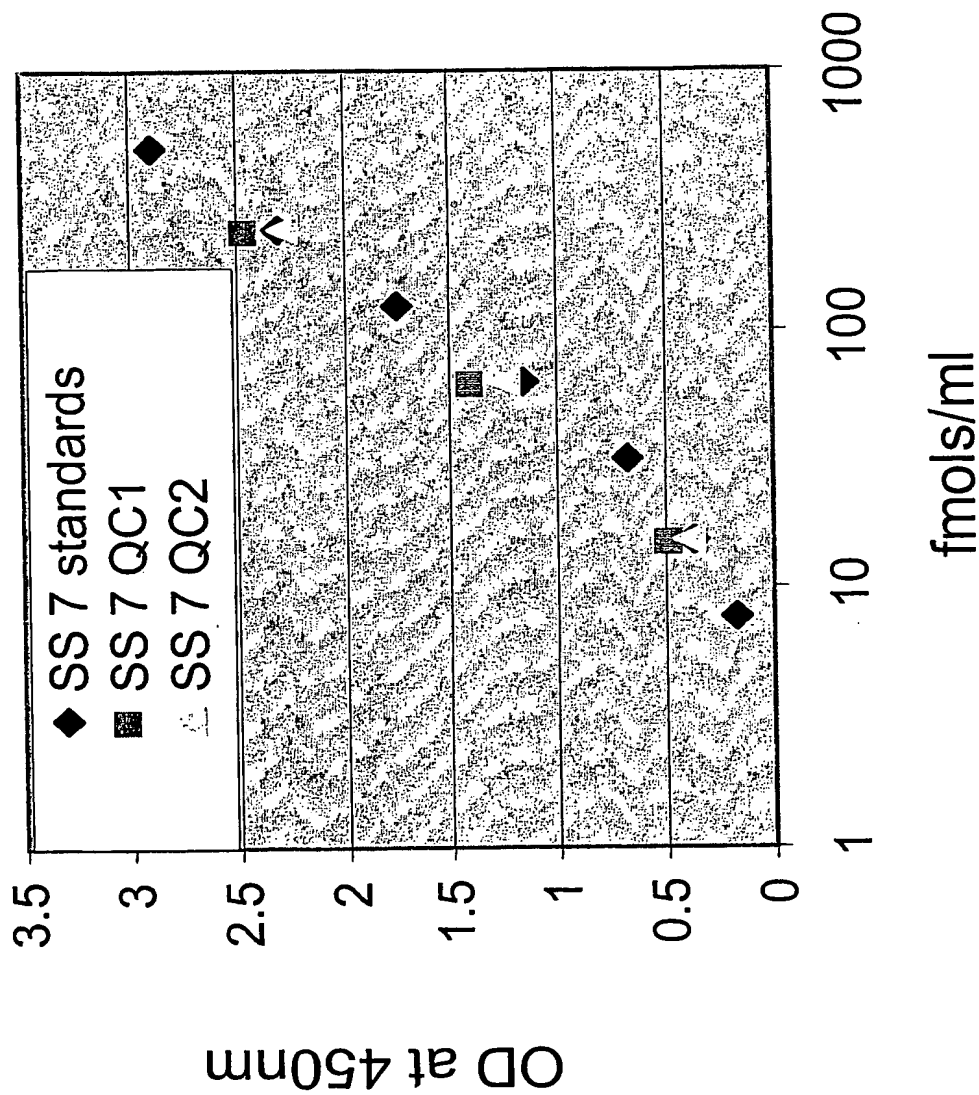
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**Figure 2D: siNA Stab 7 Trigalactose Cholesterol Conjugate Antisense Strand Standard Curve**



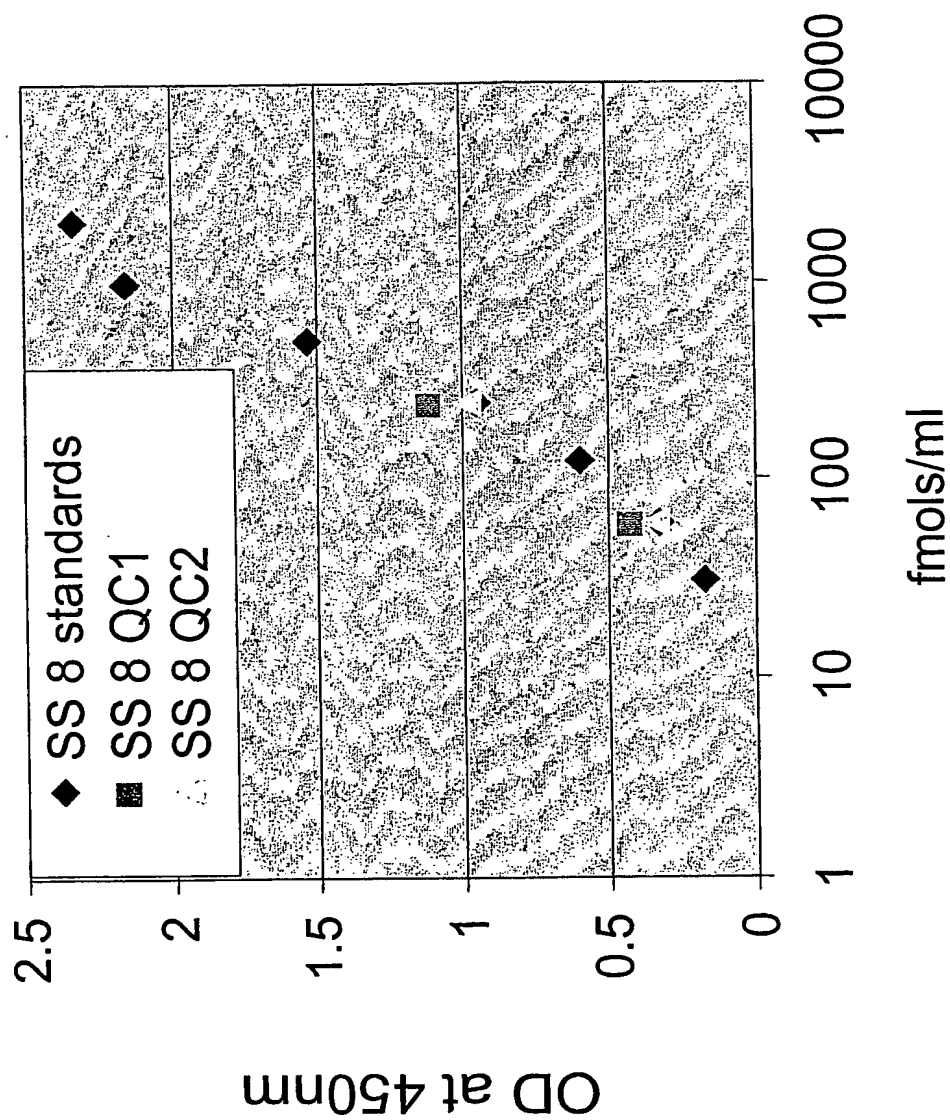
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**Figure 3A: siNA Stab 7 Single Stranded  
Quality Control Sample**



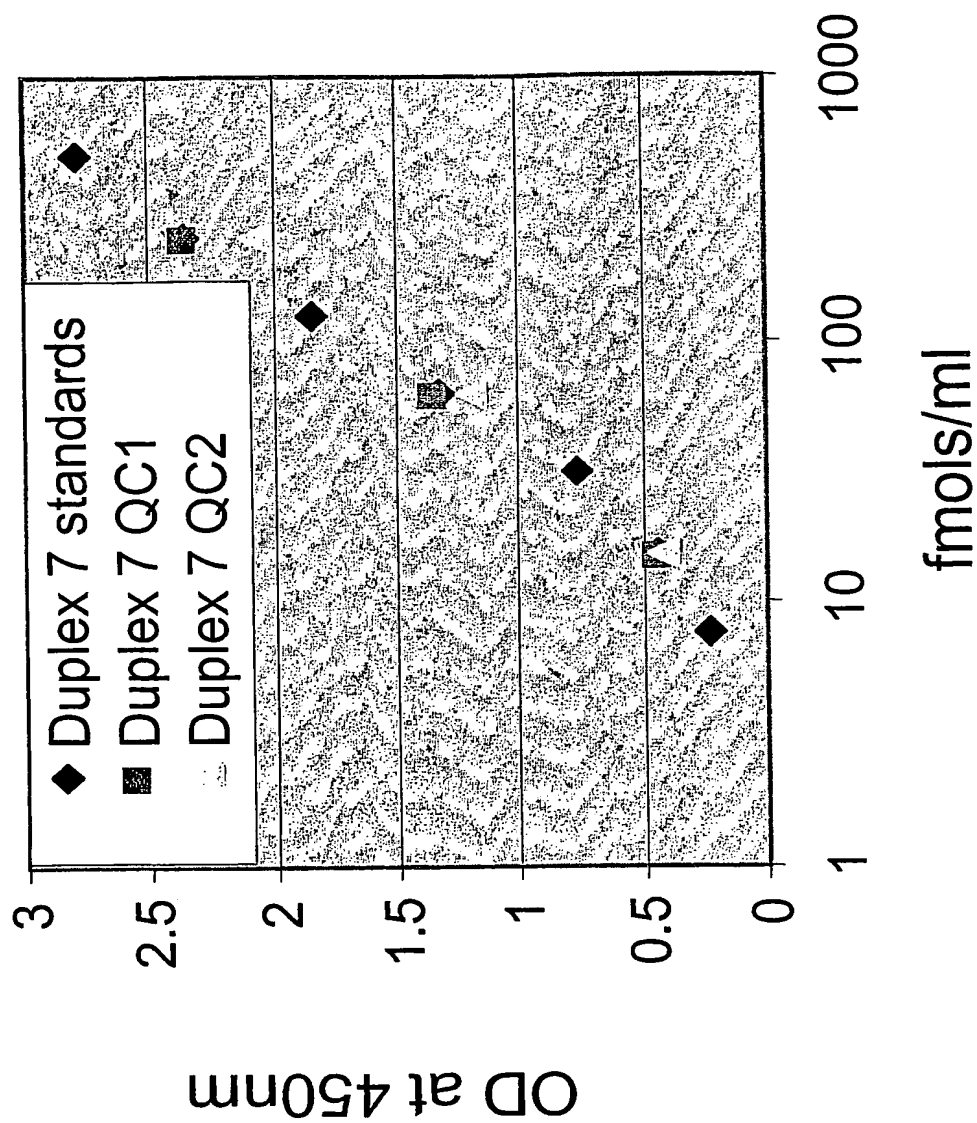
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**Figure 3B: siNA Stab 8 Single Stranded  
Quality Control Sample**



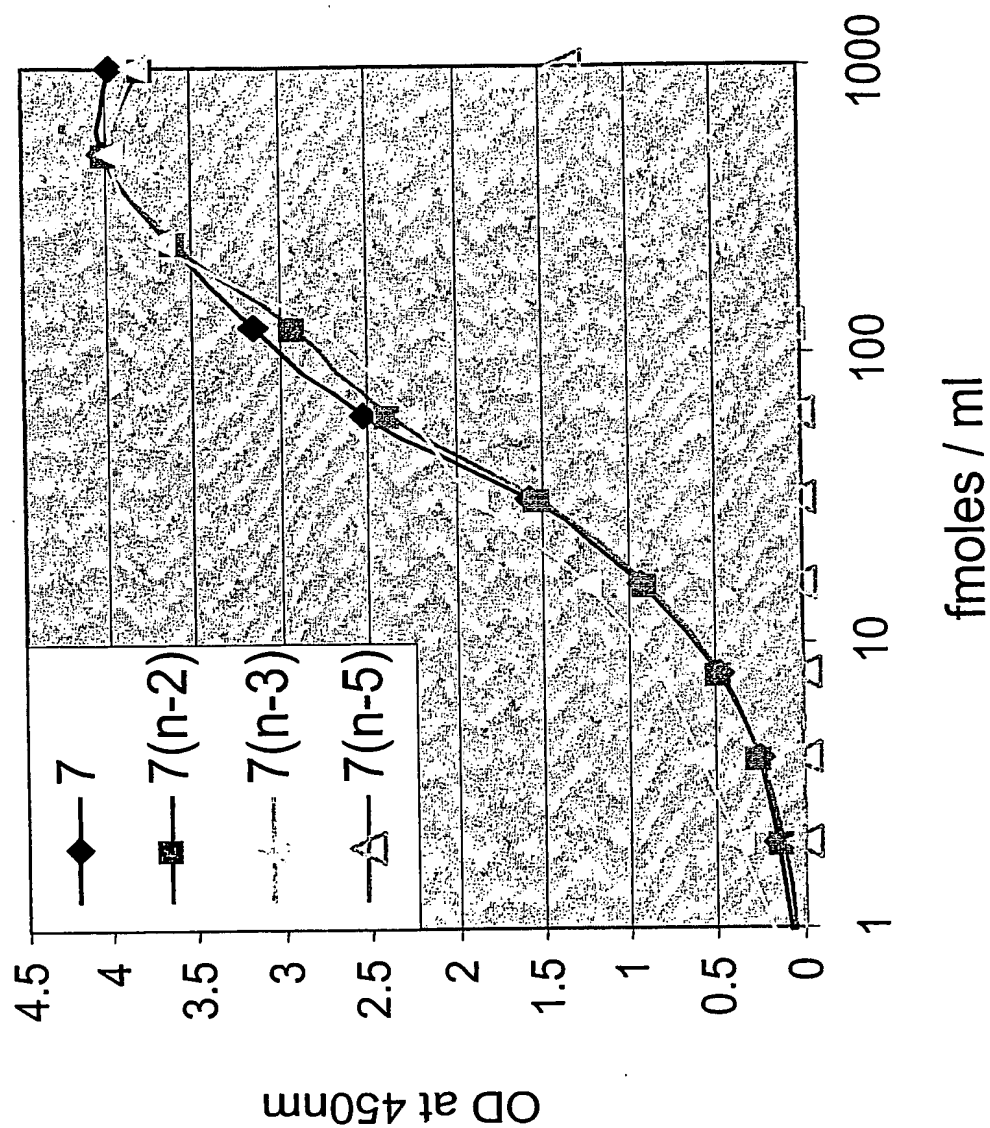
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**Figure 3C: siNA Stab 7 Duplex  
Quality Control Sample**



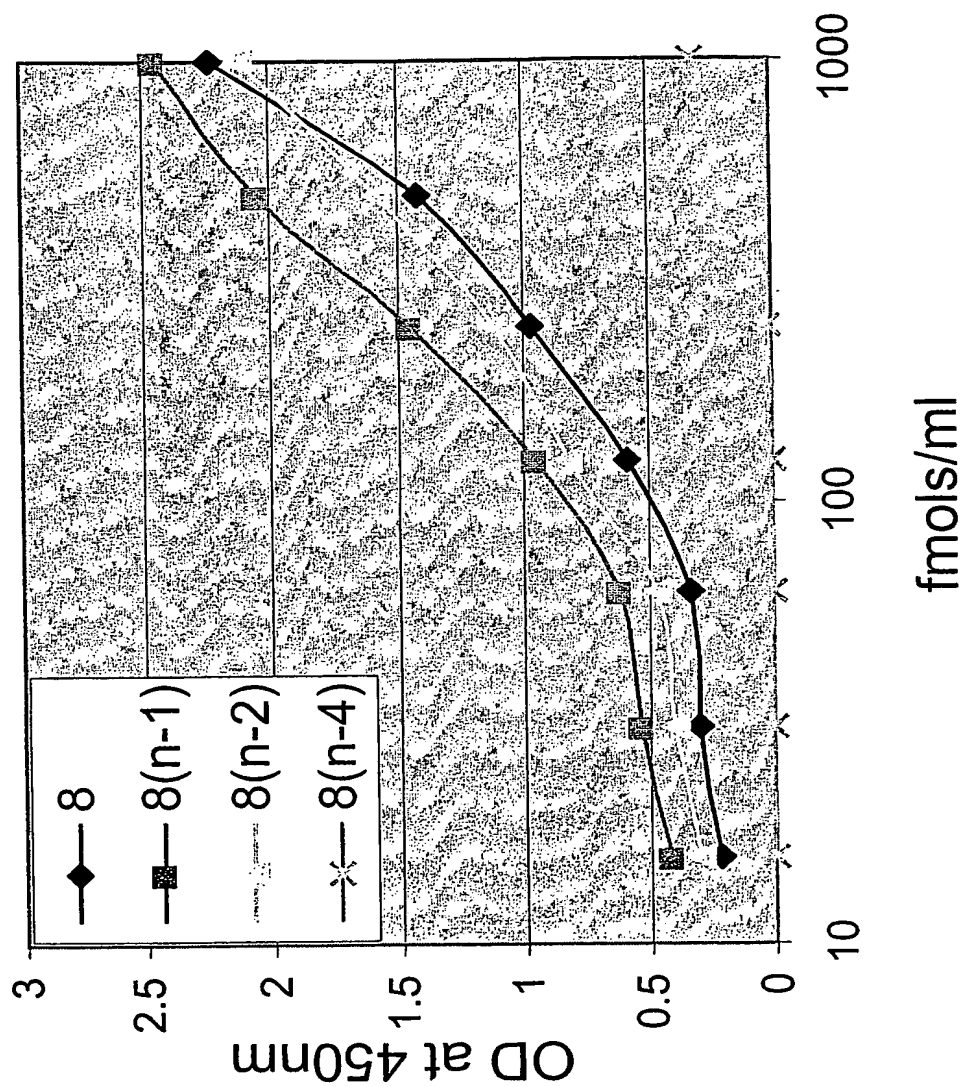
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**Figure 4A: Detection of potential  
siNA Stab 7 Metabolites via Hybridization Assay**

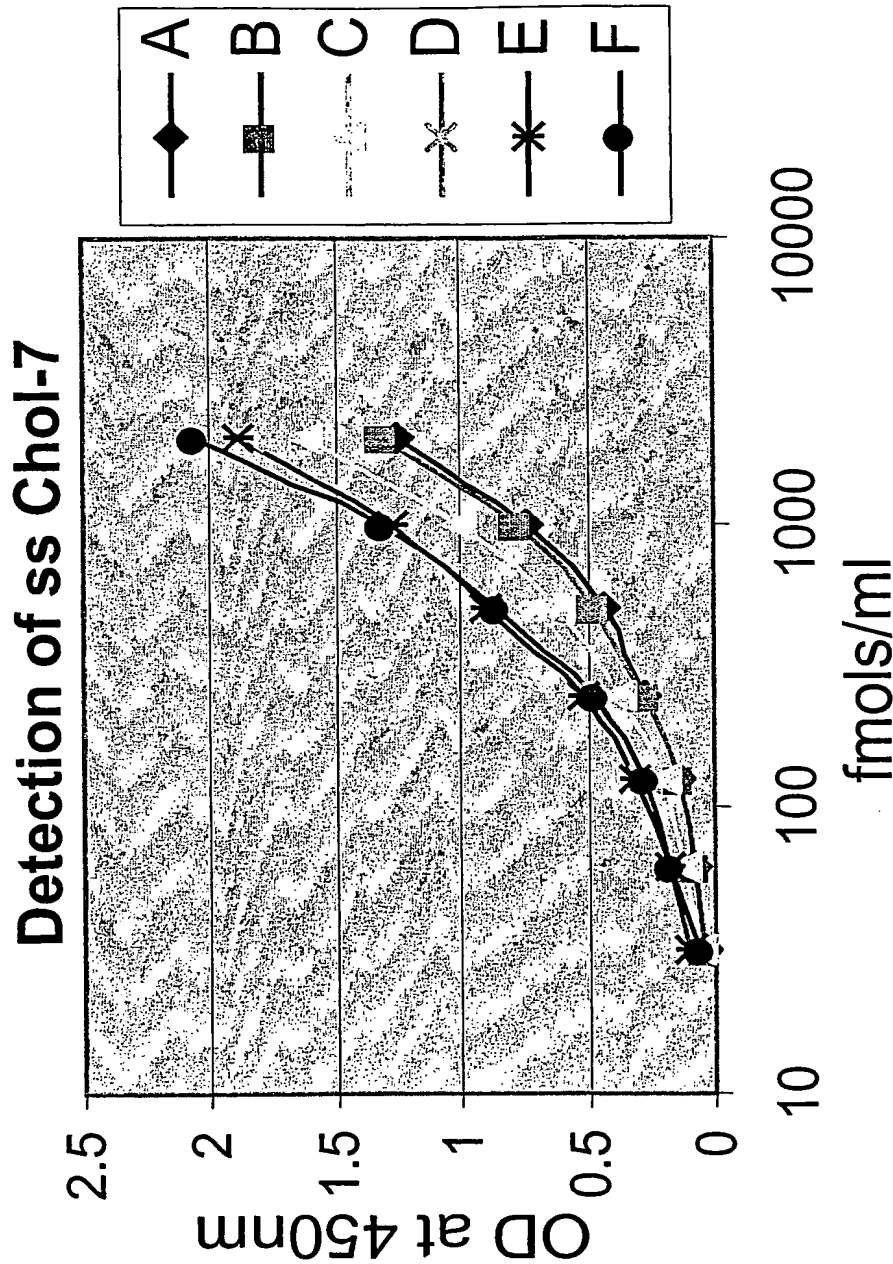


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**Figure 4B: Detection of potential  
siNA Stab 8 Metabolites via Hybridization Assay**

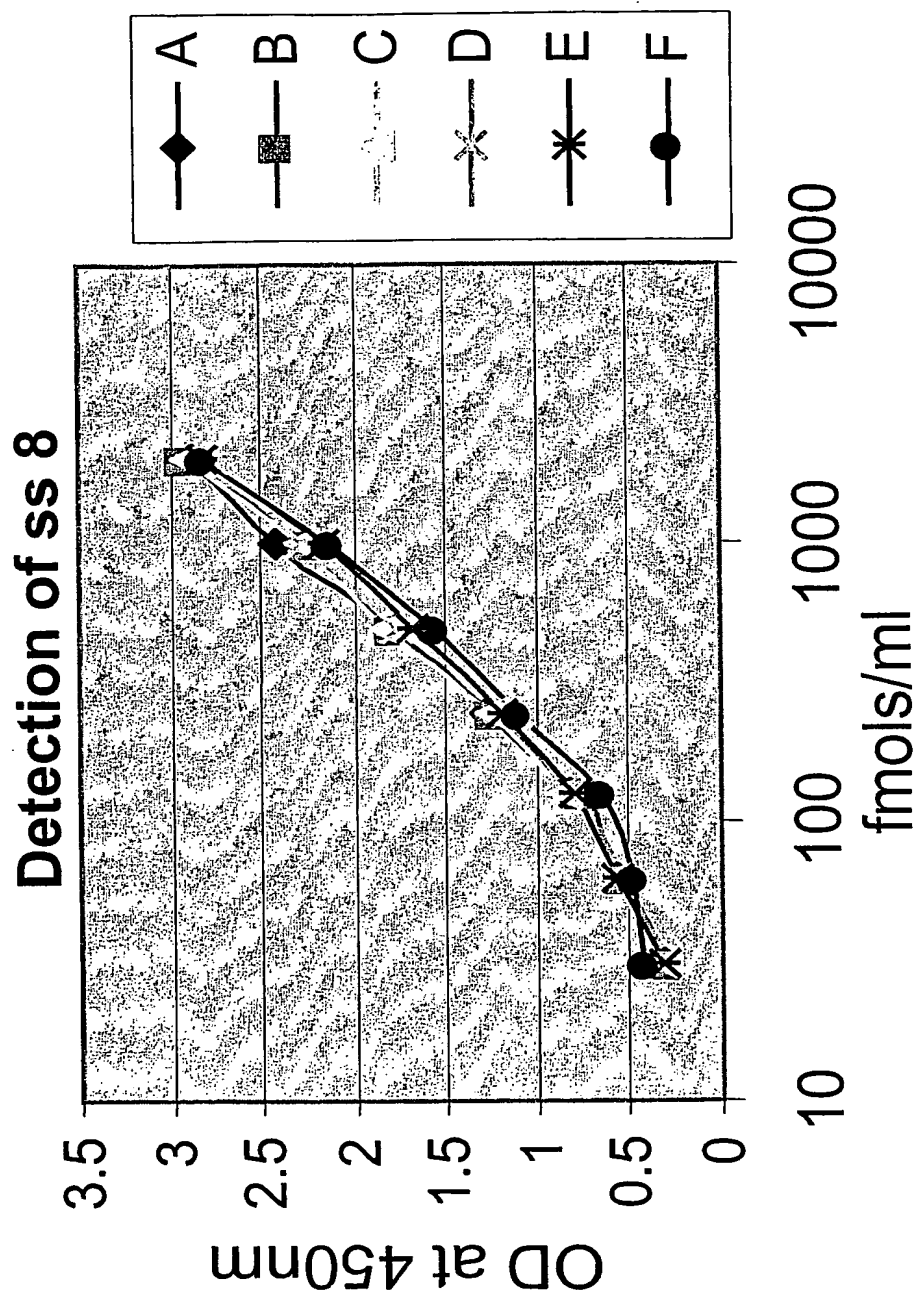


**Figure 5A: Effect of Hepatocyte lysate on detection of single stranded Stab 7 cholesterol conjugate siNA sequence**

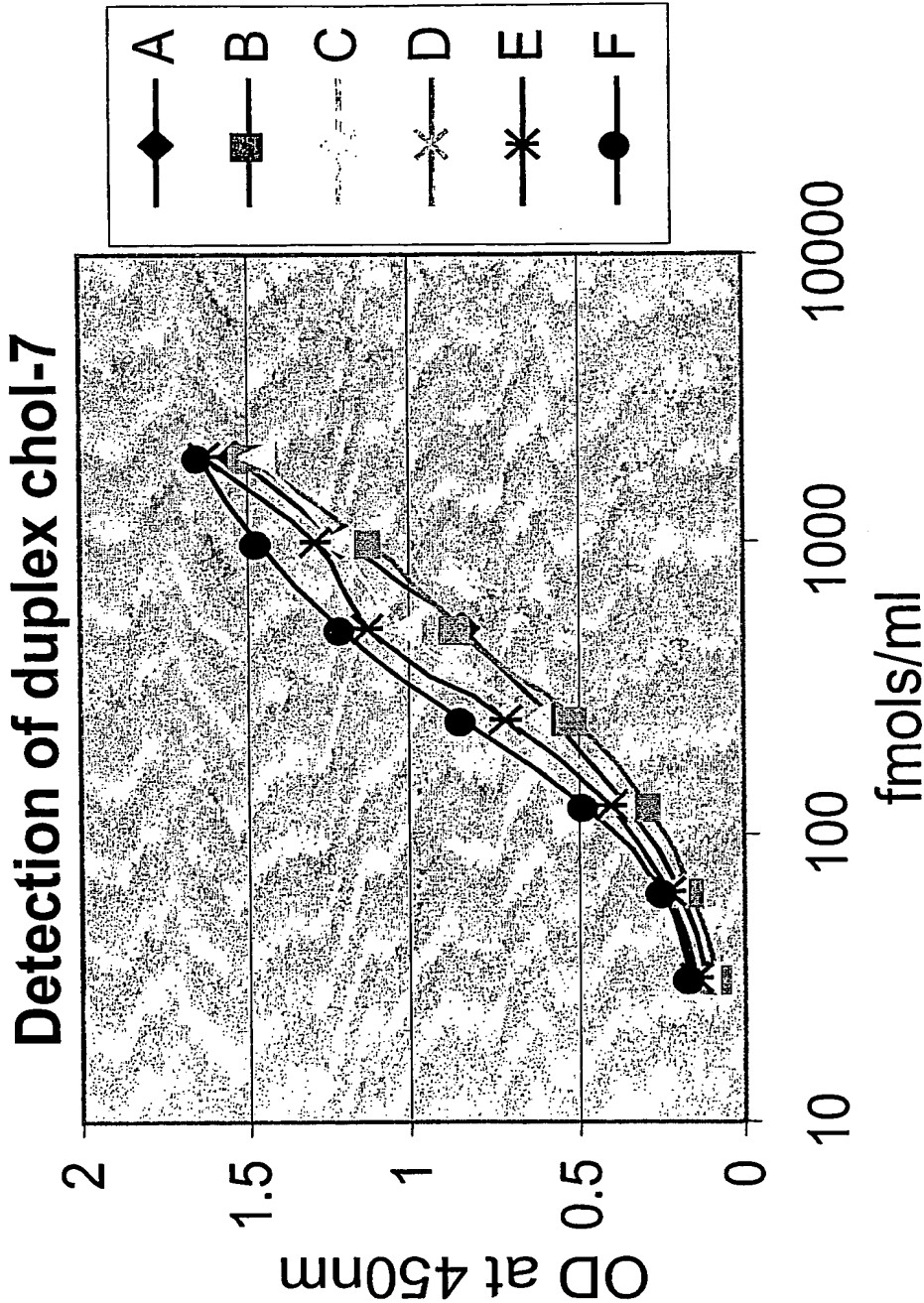


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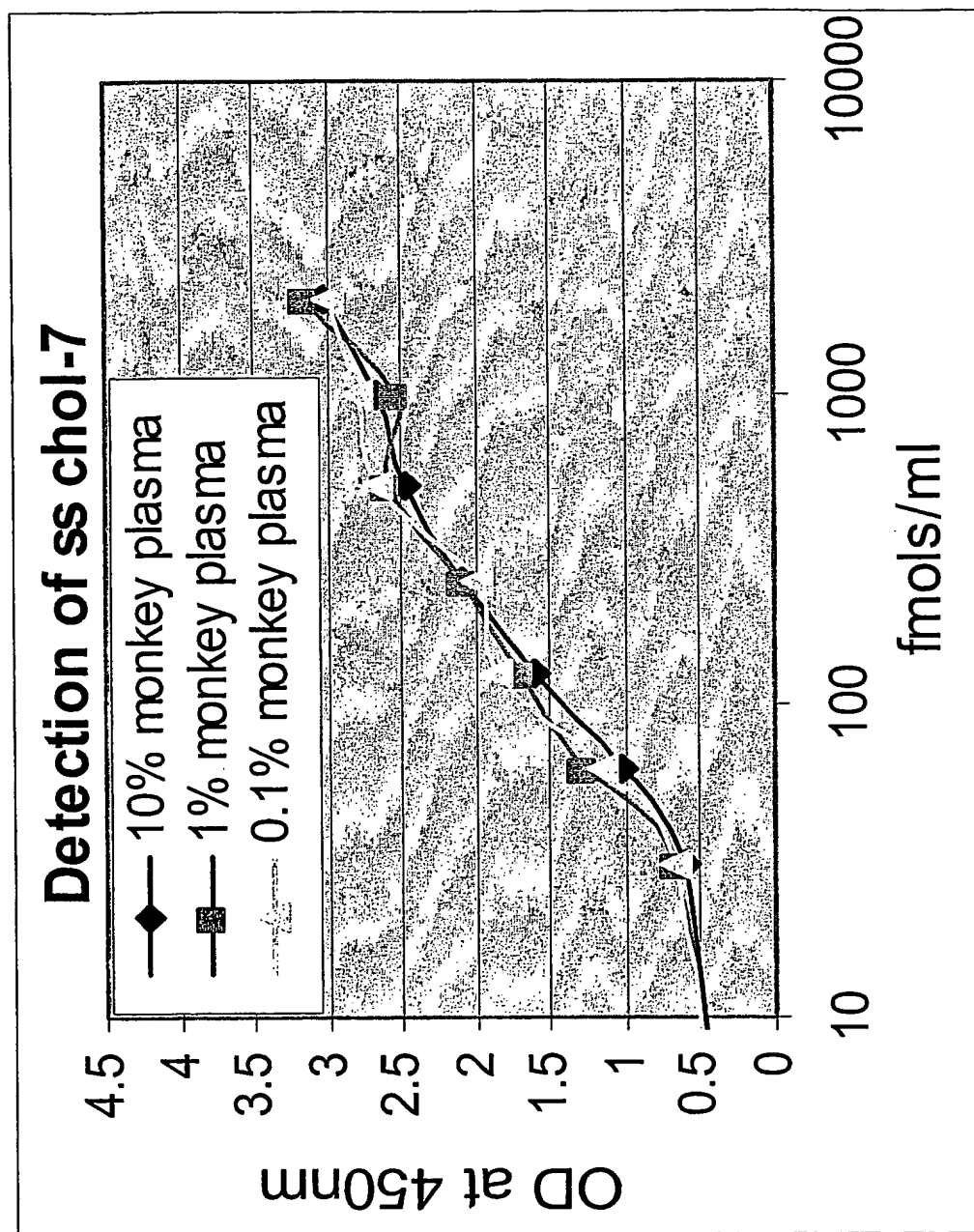
**Figure 5B: Effect of Hepatocyte lysate on detection of single stranded Stab 8 siNA sequence**



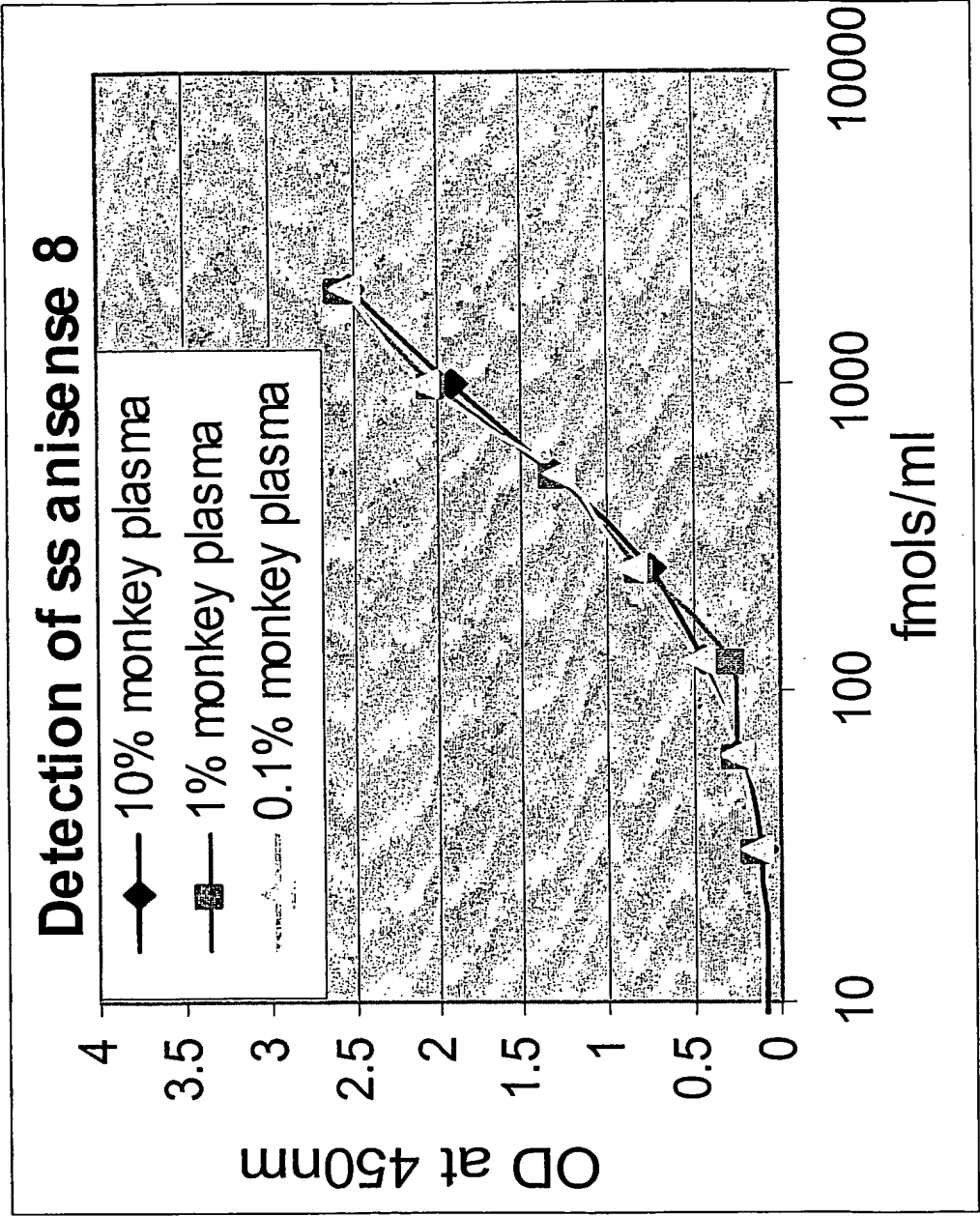
**Figure 5C: Effect of Hepatocyte lysate on detection of Stab 7 cholesterol conjugate duplex siNA sequence**



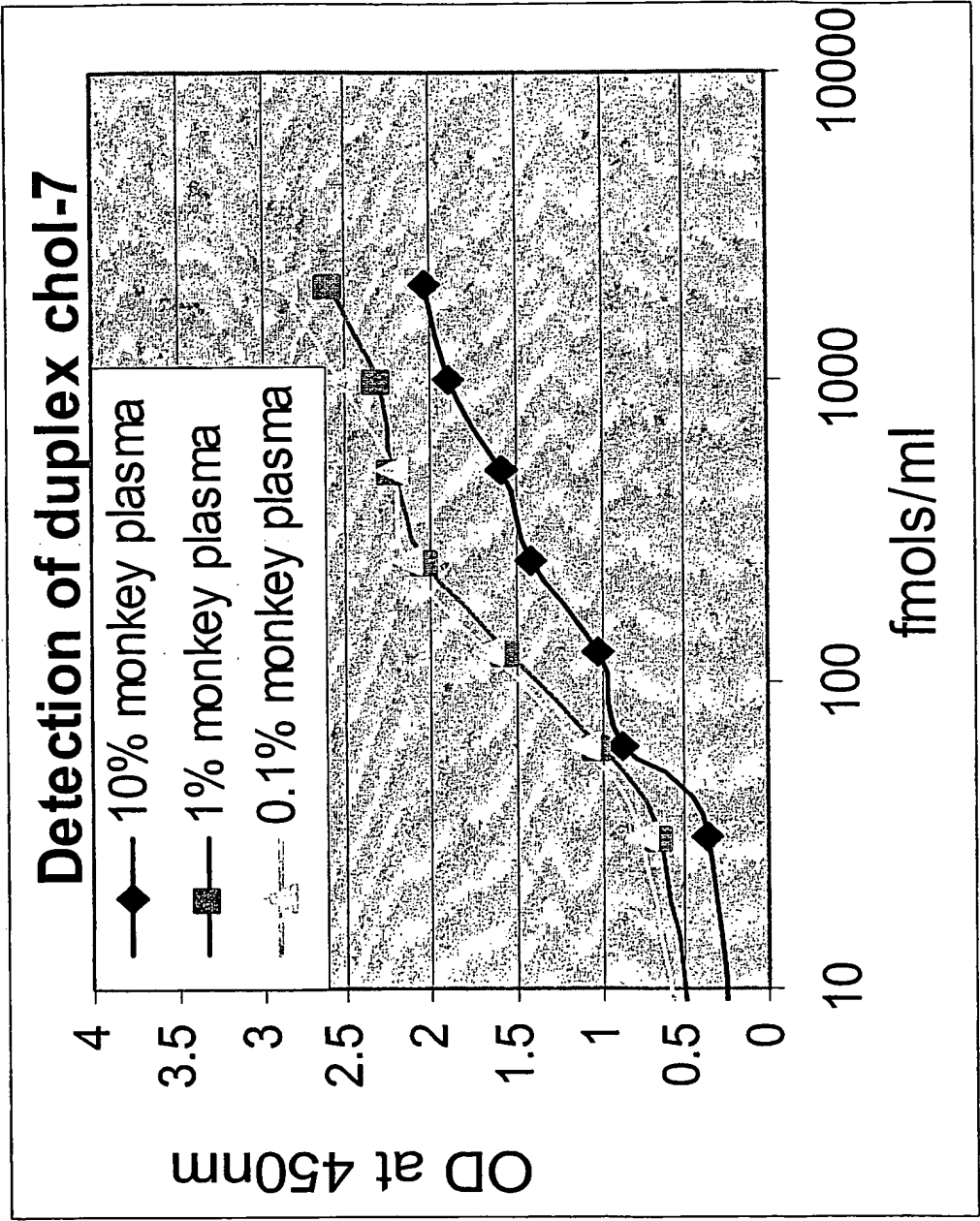
**Figure 6A: Effect of monkey plasma  
on detection of single stranded Stab 7 cholesterol  
conjugate siNA sequence**



**Figure 6B: Effect of monkey plasma on detection of single stranded Stab 8 siNA sequence**

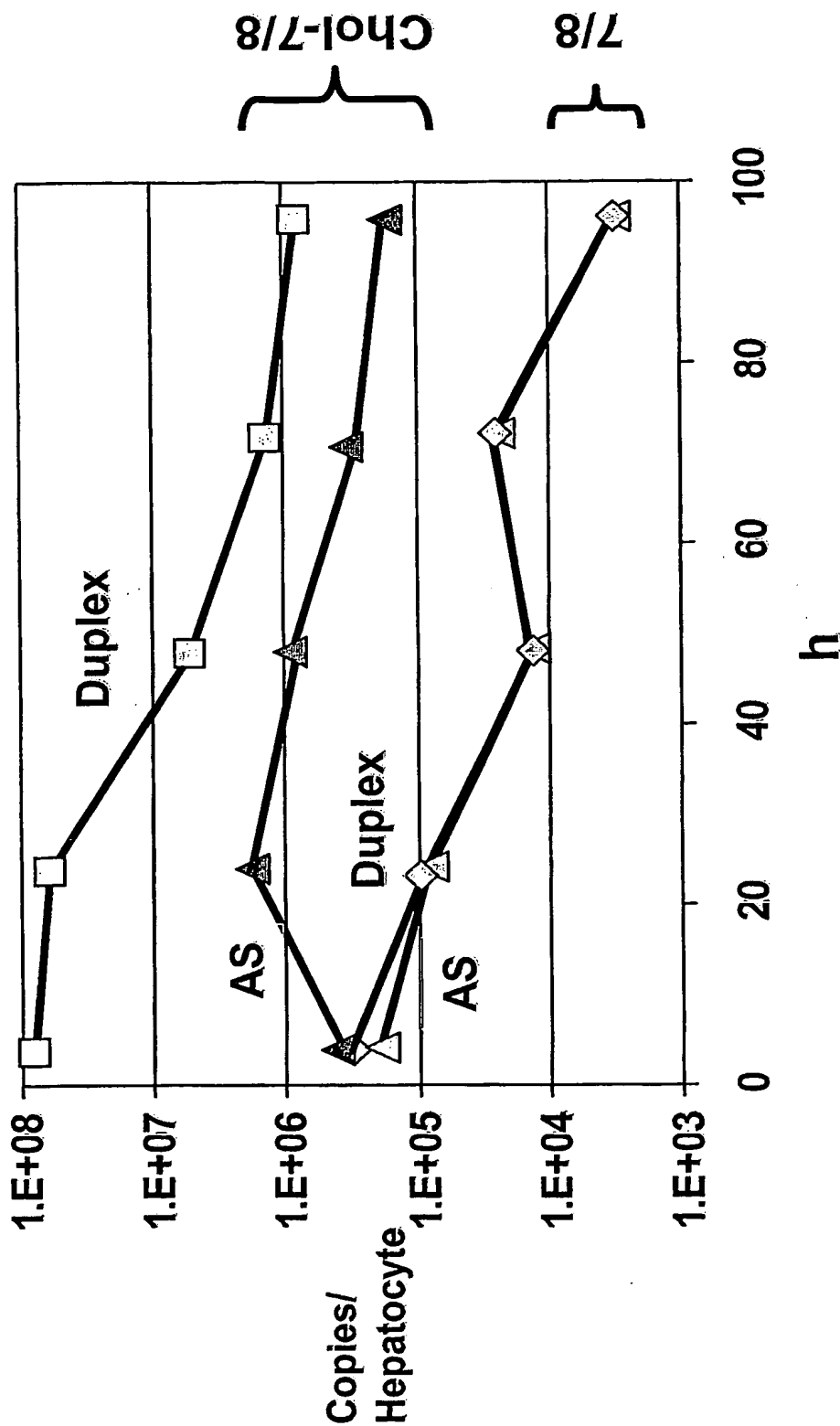


**Figure 6C: Effect of monkey plasma on detection of Stab 7 cholesterol conjugate duplex siNA sequence**



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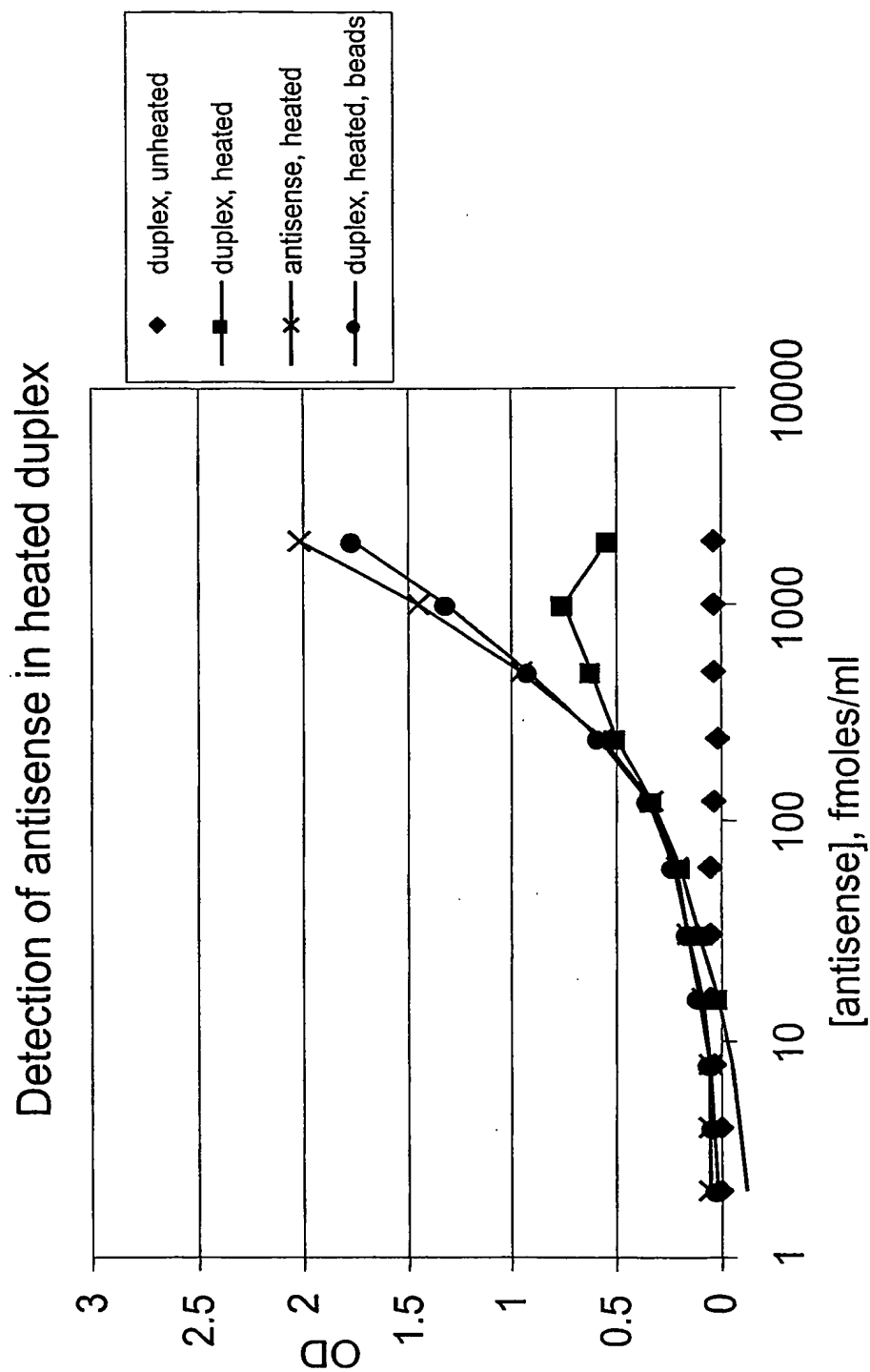
**Figure 7: Concentration of siNA duplex and antisense  
In Hepatocytes**



Given - 1 gram liver =  $1 \text{ mL} = 10^{10}$  cells [siRNA ~  $\mu\text{M}$ ]

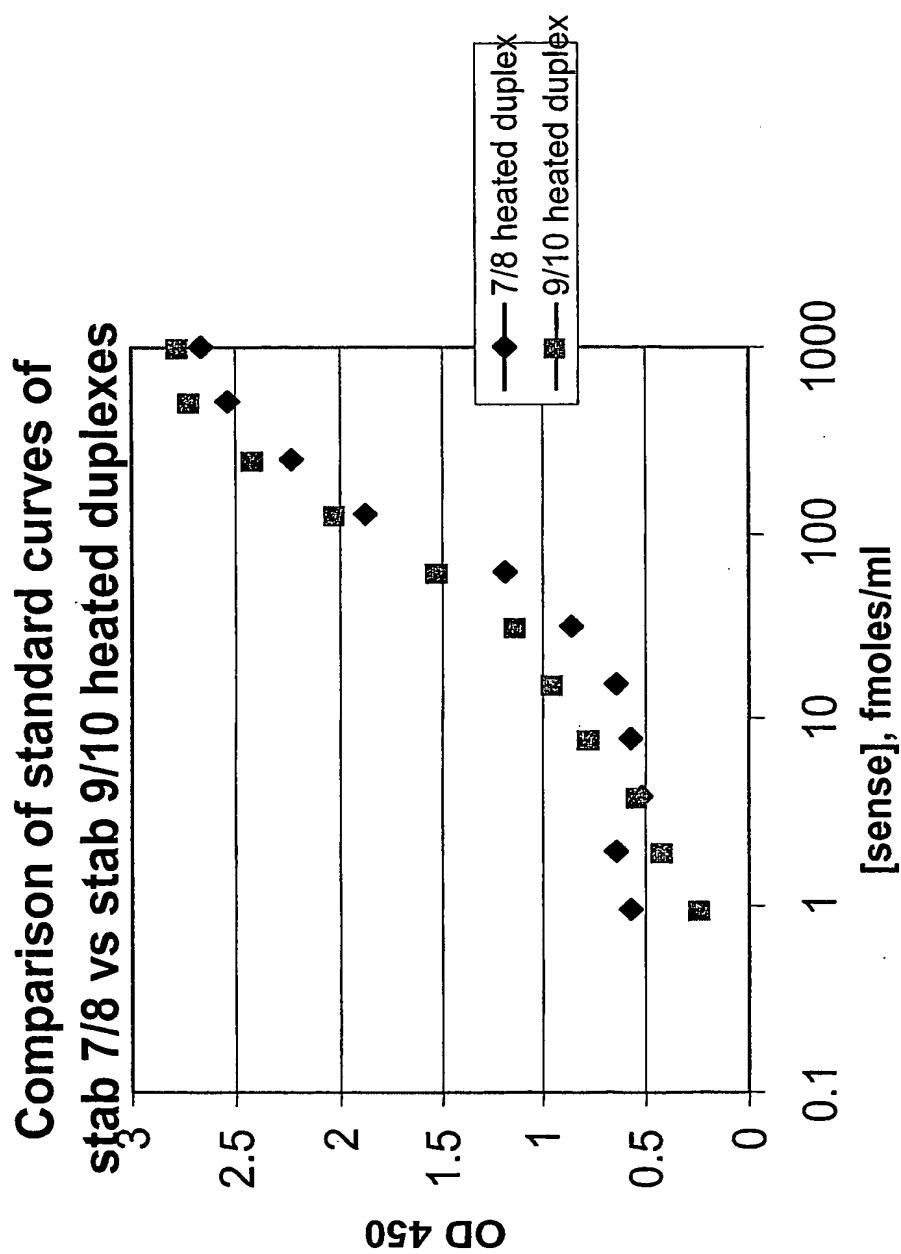
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**Figure 8: Removal of Competitive binding sequence  
In duplex assay**



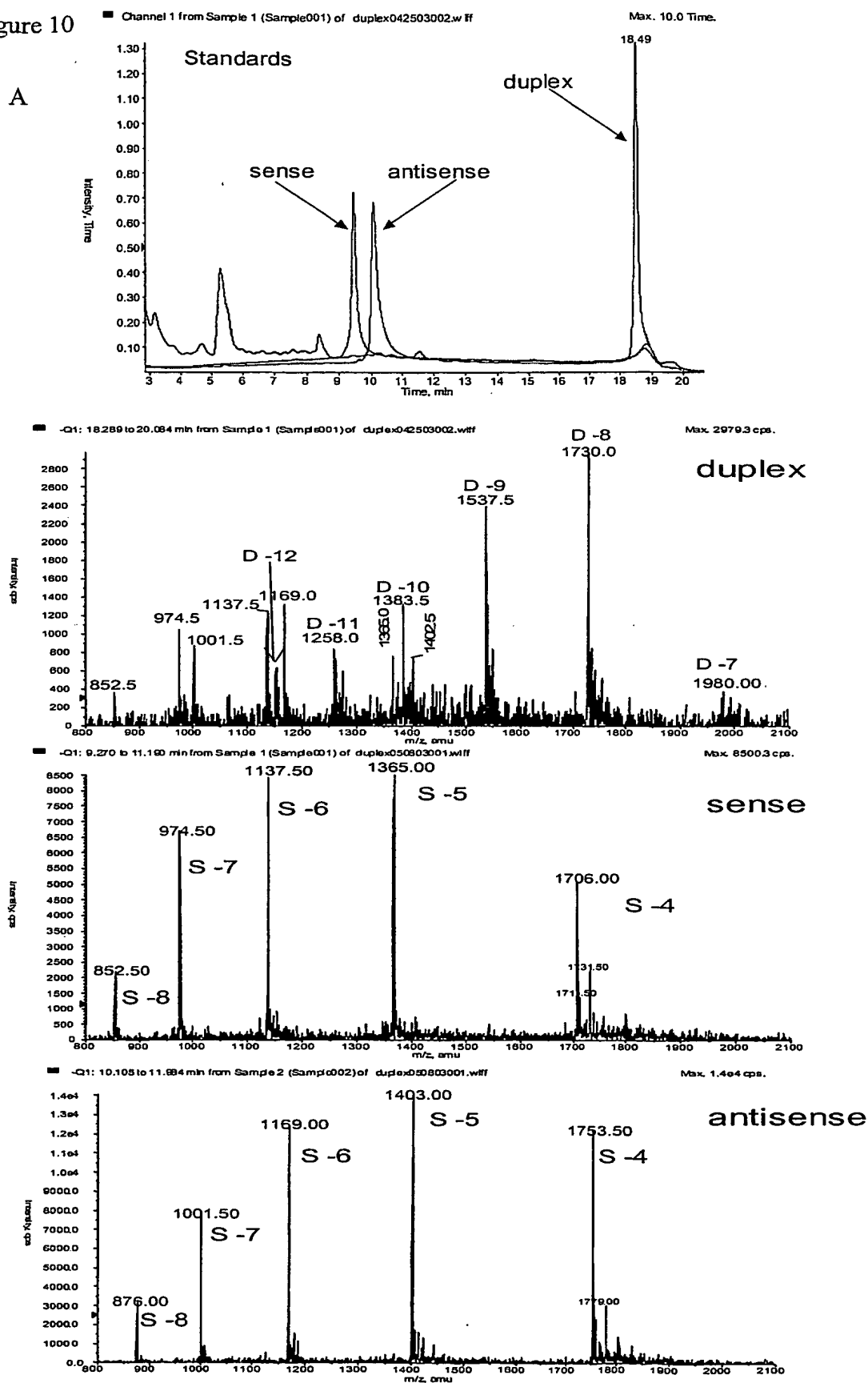
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**Figure 9: Application of Hybridization Assay to siNA molecules having identical sequences with differing chemical modifications**



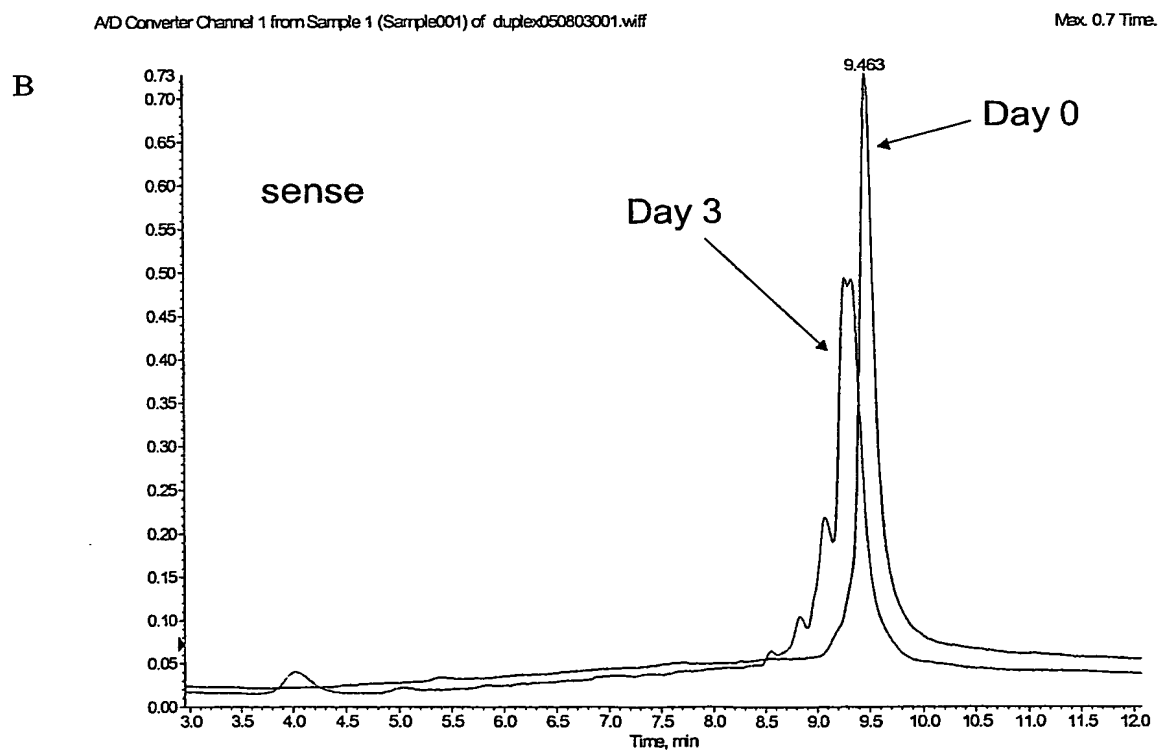
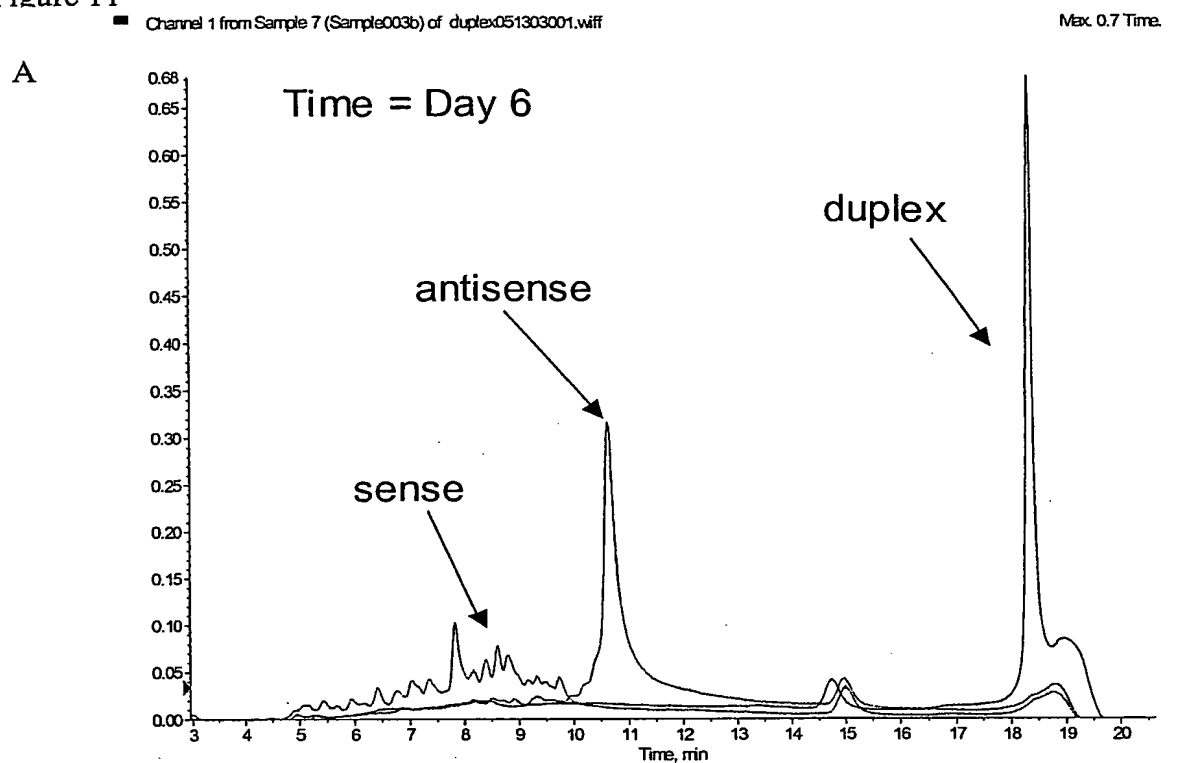
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Figure 10



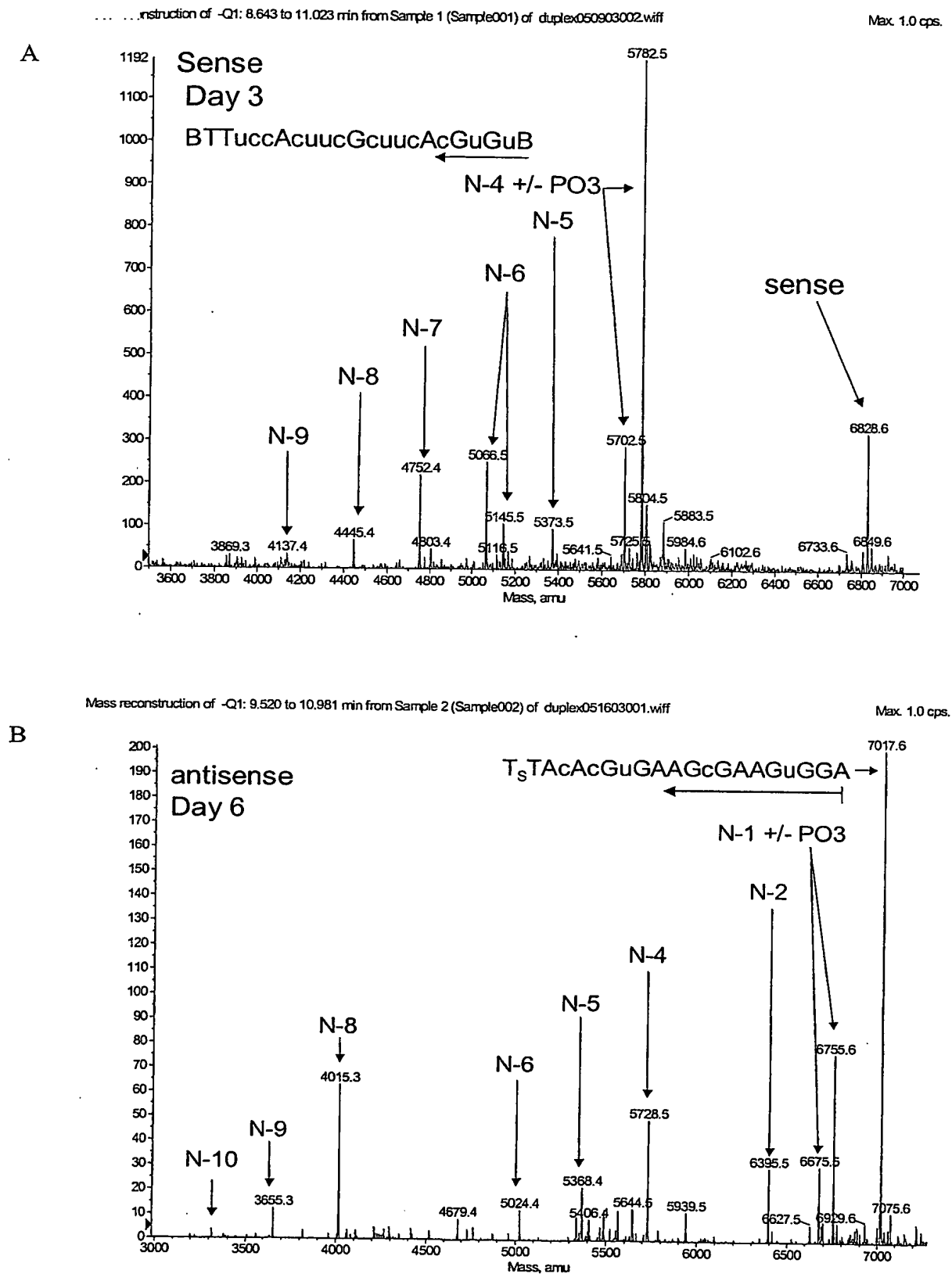
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Figure 11



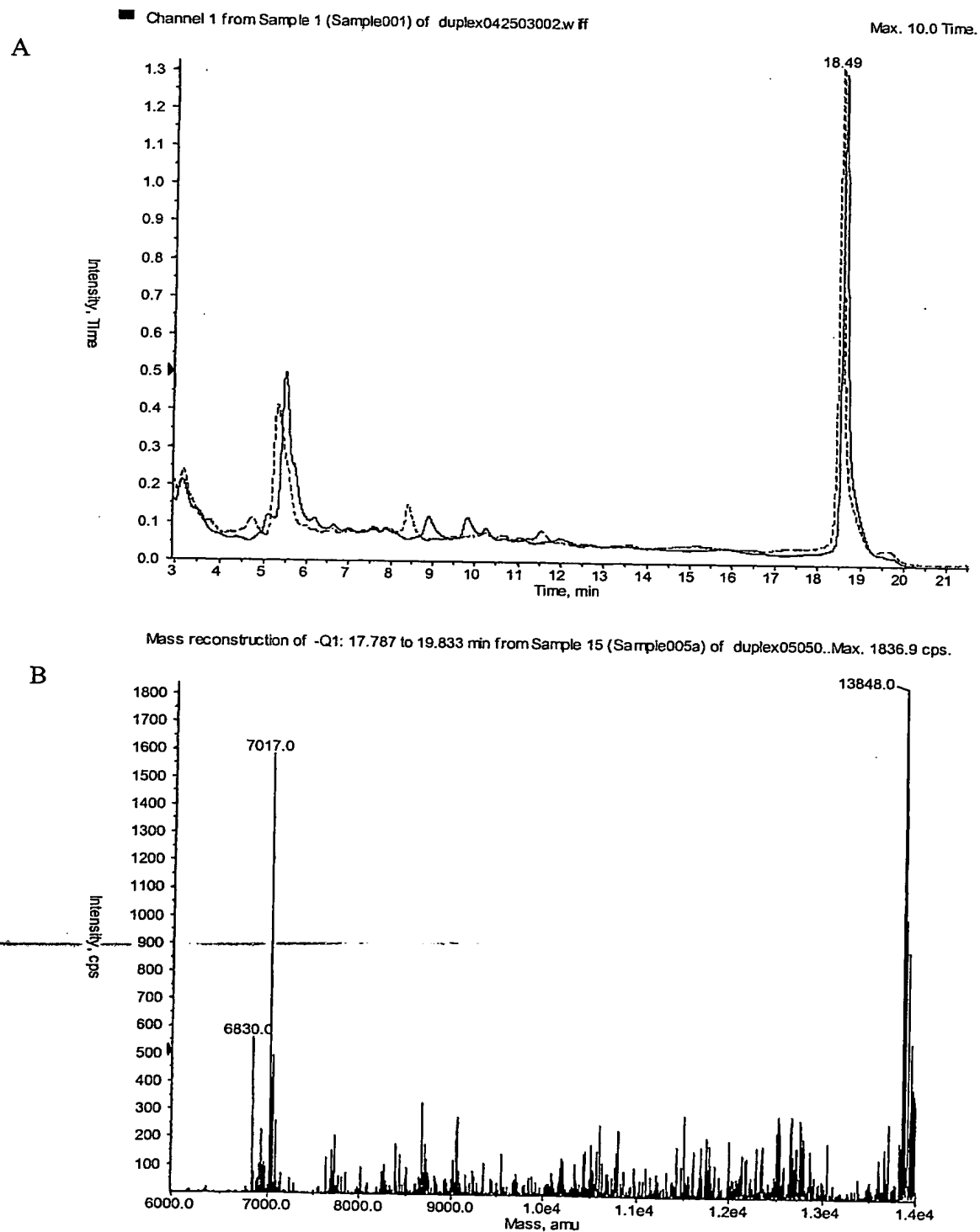
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Figure 12

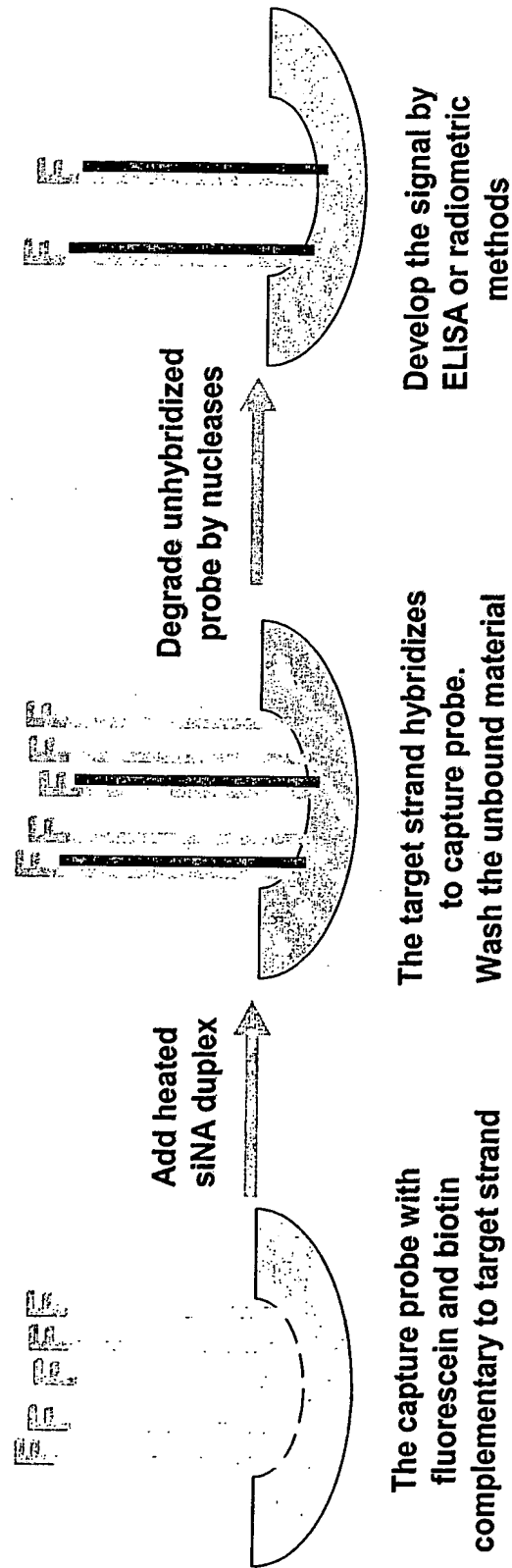


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Figure 13



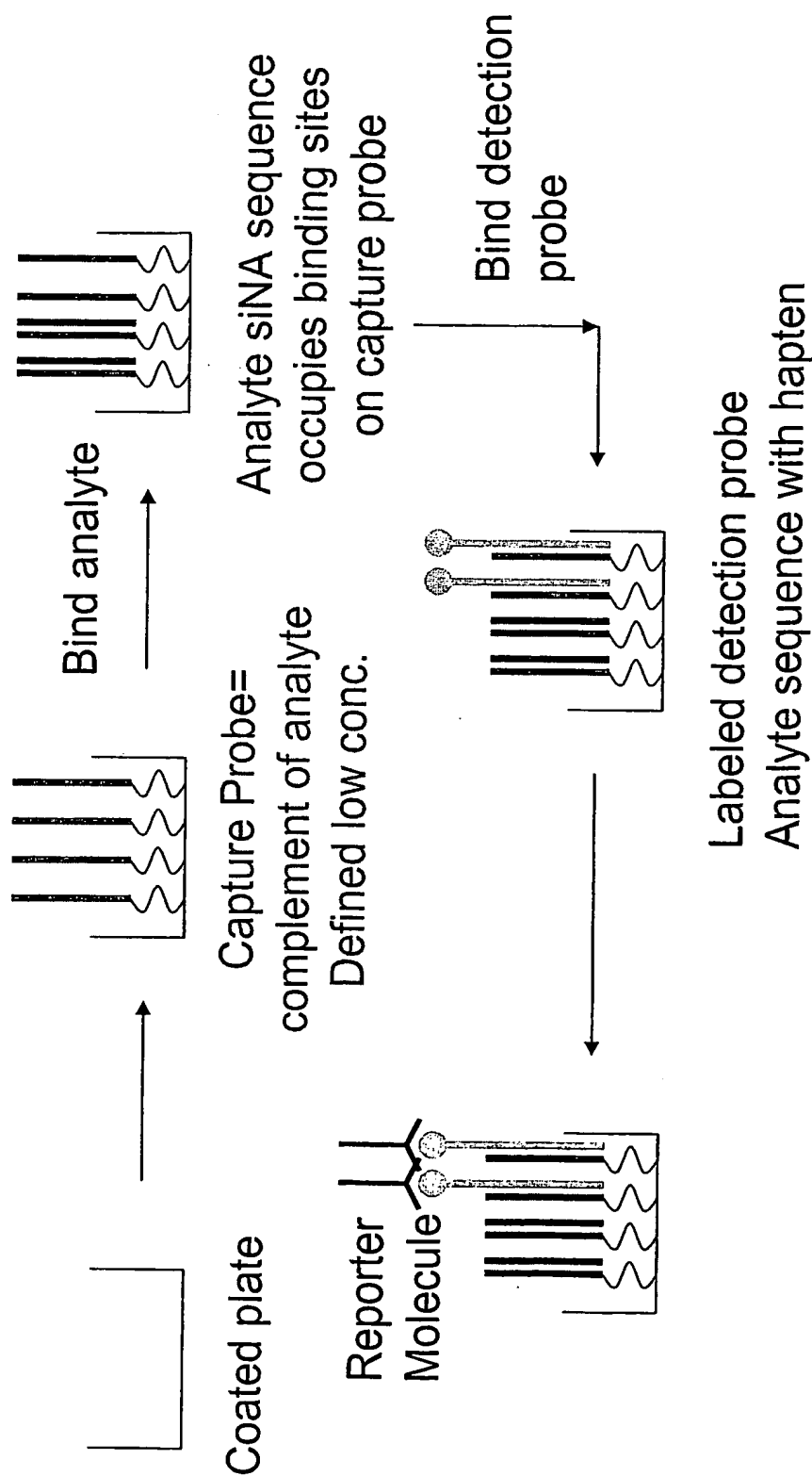
**Figure 14**



= target polynucleotide

= Labeled Capture Probe

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*Figure 15*

In this design, binding of the target siRNA (in step 1) prevents binding of a secondary detection probe (in step 2). Therefore, signal is inversely proportional to analyte concentration.

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